appear in the specification at least, *e.g.*, at page 19, lines 3-14. Support for further amendments to claim 29 appears in the specification, *e.g.*, at least at page 6, lines 19-21, and in FIG. 1 as originally filed. No new matter has been added.

Claims have be objected to and rejected on various grounds. Each will be addressed in turn below.

Claim Objections

Claims 5, 6 and 14 have been objected to for containing typographical errors or for being in improper dependent form. Claim 6 has been cancelled. Claims 5 and 14 have been amended to place them in proper dependent form. No new matter has been added by these amendments. Withdrawal of these objections is hereby requested.

Claim Rejections

Examiner's Position

In the Office Action dated December 28, 2001, the Examiner made the following rejections:

(1) Claims 1-10, 19-21 and 28-29 were rejected under 35 U.S.C. §101 as not supported by a specific, substantial, or credible utility;

(2) Claims 1-10, 19-21 and 28-29 were rejected under 35 U.S.C. §§ 101, 112, first paragraph, for failing to adequately teach one skilled in the art how to use the claimed invention;

(3) Claims 1-10, 14, 19-21 and 28-29 were rejected under 35 U.S.C. §112, first paragraph, for lack of written description;

(4) Claims 1, 3-4, 19-21 and 28 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite; and

(5) Claims 5-6 and 28-29 were rejected under 35 U.S.C. §102(b), for being anticipated.

Applicants traverse each of these rejections and address each individually as follows.

The § 101 rejections; Combined §§ 101, 112 rejections

Claims 1-10, 19-21 and 28-29 have been rejected under 35 U.S.C. § 101 alone, and under the combination of 35 U.S.C. § 101 and 35 U.S.C. §112 para 1, as not being supported by either a specific and substantial credible asserted utility or a well-established utility. According to the Examiner, "the instant application does not disclose the biological role of the nucleic acid, the encoded protein or the significance of either." (Office Action at p. 4). The Examiner further characterizes these claims as failing to adequately teach how to use the instant invention. (Office Action at page 8). Applicants traverse these rejections for the reasons described below.

Applicants present a Declaration under 37 CFR 1.132 (Exhibit 1), showing the data that the FGF protein of the instant invention induces DNA synthesis (as measured by bromodeoxyuridine incorporation) in NIH 3T3 mouse fibroblasts in a dose dependent manner (Exhibit 1, Figure 1, Panel A). In addition, FGF protein also induced DNA synthesis in human cell lines CCD-1070Sk normal human skin fibroblasts (Exhibit 1, Figure 1, Panel B) and CCD-1106 keratinocytes (Exhibit 1, Figure 1, Panel C). These results indicate that the FGF-CX protein of the present invention facilitates not only cell growth, but cell proliferation in, *e.g.*, at least fibroblasts, a cell type involved in many human proliferation-associated disorders. Applicants' disclosure of FGF-CX's role in cell growth and proliferation is thus fully supported by experimental evidence, and is a credible, substantial and specific utility. FGF-CX's biological activity is the same as what is disclosed in the specification. The utility and written description rejections simply do not apply.

One of the key events in cancer is uncontrolled proliferation, and thus the FGFs exhibiting mitogenic activity (like FGFs 1-10, 16-18, 20) may be involved in tumorigenesis via direct deregulated growth stimulation of cancer cells in an autocrine, paracrine or juxtacrine fashion. Applicants present the data showing induction of cell proliferation by FGF protein of the instant invention (Exhibit 1, Figure 2, Panel D). Herein, NIH 3T3 cells cultured with FGF protein showed 3-fold increase in cell number as compared to the control, demonstrating a role in cell proliferation. These results presented by the applicants support a credible, substantial and specific utility for the instant invention.

The examiner has pointed out that the disclosed protein 'only shares approximately 70% amino acid sequence similarity/identity with the most closely related protein of the prior art'. The polypeptides of the present invention are characterized as members of the FGF family of

proteins based on homology. The Utility Examination Guidelines state that " When a class of proteins is defined such that the members share a specific, substantial and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same, specific, substantial, and credible utility to the assigned protein" Fed. Reg., Vol. 66. No. 4, January 5, 2001, p. 1096. The disclosed protein is 100% identical to human FGF-20 (SWISSPROT-ACC:Q9NP95 release date: 16 October, 2001), 95% identical to rat FGF-20 (SPTREMBL-ACC:Q9EST9), 94% identical to mouse FGF-20 (SPTREMBL-ACC:Q9ESL9) (Exhibit 2: ClustalW Alignment).

Although the FGF family is diverse and complex according to Galzie et al (provided by the examiner), the applicants would like to point out that Galzie et al does not discuss or mention FGF-20, which is 100% identical to the protein of the instant invention and thus cannot support a case for lack of utility of the present invention.

Consistent with the teachings of the specification, the utilities known by those of ordinary skill in the art, and the data presented in the attached Exhibits, applicants respectfully submit that it is clear that the FGF-CX nucleic acids and the encoding polypeptide of the present invention can be used as markers for, *e.g.*, cancer and angiogenesis, and thus has credible, specific and substantial utilities. Applicants assert that the functional attributes of the FGF family members are the functional attributes asserted by applicants for SEQ ID NOs: 1 and 2 in the specification. Accordingly, applicants submit that the claimed invention has a utility that is credible, substantial and specific to the FGF family of proteins and therefore respectfully request withdrawal of the rejection based on 35 USC §101, either alone or in combination with §112 para 1.

The § 112, first paragraph rejections

Utility-Based Rejections

Claims 1-10, 19-21 and 28-29 have been rejected under 35 U.S.C. § 112, first paragraph, in view of the 35 U.S.C. § 101 rejection, ostensibly because one skilled in the art would not know how to use an invention that has no utility. Applicants traverse this rejection. As described above, claims 1-10, 19-21 and 28-29 do have a specific, substantial, and credible utility as novel markers fore, *e.g.*, cancer and angiogenesis. Because the claims have such utility, Applicants submit that they are enabled. Thus, the rejection of these claims should be withdrawn.

Written Description-Based Rejections

Claims 1-10, 14, 19-21 and 28-29 have been rejected under 35 U.S.C. § 112, first paragraph, for what is characterized as subject matter described in the specification in a manner that does not reasonably convey to one skilled in the art that the Applicant had possession of the claimed in invention at the time the application was filed. Claims 2-10, 14 and 19-21 depend directly or indirectly from claim 1. Claim 29 depends from claim 28. Therefore, discussion of claims 1 and 28 will by necessity include all dependent claims. Applicants traverse the rejection as applied to the claims as amended.

The Examiner states that claims 1 and 28 do not have sufficient written description for "polynucleotides encoding polypeptides having 85% sequence identity to SEQ ID NO:2" and "derivatives, analogs, homologs and allelic variants of SEQ ID NO:1". Without acceding to the propriety of the Examiner's position, and in order to expedite prosecution, Applicants have amended the claims so that they no longer recite 85% sequence identity or derivatives, analogs, homologs and allelic variants. Accordingly, Applicants believe that these rejections have now been rendered moot and request that such rejections be withdrawn.

The Examiner has specifically rejected claim 14 for failing to teach how a FGF-CX polypeptide can be produced by a complementary nucleic acid sequence. Applicants have amended claim 14 to recite that the FGF-CX polypeptide is defined by the amino acid sequence provided in SEQ ID NO:2. It is now very clear to one skilled in the art which strand is to be used to produce the FGF-CX polypeptide of the invention. This rejection is now moot, and Applicants respectfully request that it be withdrawn.

The Examiner has rejected Claim 29 because "the nucleic acids by themselves do not have activity". Applicants have amended this claim to clarify that it is the polypeptide encoded by the nucleic acid that is associated with the activities claimed. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The § 112, second paragraph rejection

Claims 1, 3-4, 19-21 and 28 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claim 3 has been cancelled and thus is not under consideration. Claim 21 has been withdrawn from further examination, as it is directed to a non-

elected invention, as indicated by the examiner. Applicants traverse the rejection as applied to the remaining claims as amended.

Claims 1 and 28 have been rejected for referring to the invention as "FGF-CX", which is characterized as indefinite. These claims have been amended to specify that FGF-CX is defined by the sequences in SEQ ID NOs:1 and 2. These amendments remove what the Examiner characterized as an indefinite recitation of FGF-CX. This rejection is now moot and withdrawal is respectfully requested.

Claims 4 has been rejected because the phrase "hybridizing ... under stringent conditions" is characterized as being indefinite. However, Applicants note that, *e.g.*, on page 17, line 9, the specification clearly describes stringent conditions as, "conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other." Actual embodiments of stringent conditions are provided, *e.g.*, at least on page 18, lines 1-8 Thus Applicants respectfully request that the Examiner withdraw this rejection.

Claims 19-20 have been rejected for reciting "a therapeutically or prophylactically effective amount." Without acceding to the propriety of the Examiner's position, and in order to expedite prosecution, Applicants have amended the claims so that they no longer recite this phrase. Accordingly, Applicants believe that the rejection is now moot and request that it be withdrawn.

The §102(b) rejection

Claims 5-6 and 28-29 have been rejected as being anticipated by Nauro et al. (U.S. Pat. No. 5,512,460). Claim 6 has been cancelled to expedite prosecution. Applicants traverse the rejection as applied to the claims as amended.

Amended claim 5 now requires that conservative amino acid substitution be made within the context of SEQ ID NO:2, without altering the functional ability of the FGF-CX polypeptide. Amended claims 28 and 29 no longer recite "derivatives" or "analog" or "homolog" or "fragments" of FGF-CX. As stated by the Examiner, the sequence disclosed by Nauro *et al.* does not encode FGF-CX, but could be considered a "derivative, analog, or homolog." Since these terms are no longer recited in claim 28, and do not appear in claim 5, the disclosed Nauro *et al.*, sequence does not set forth each and every element of the claimed invention. Accordingly,

Applicants submit that claims 5 and 28-29 are not anticipated by Nauro et al, and request that the Examiner withdraw all §102(b) rejections.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance, and request an action be issued to this effect. With the accompanying Petition for a Three-Month Extension of Time and fee, these documents are due on or before June 28, 2002. The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 15966-557 (Cura-57).

If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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Dated: June 28, 2002

Appendix A: Version Marked to Show Changes Made in Abstract

In the specification:

Amend the Abstract on page 81 as indicated below.

The present invention provides FGF-CX[, a novel newly isolated polypeptide, as well as a polynucleotide encoding FGF-CX] polypeptides and polynucleotides, and antibodies that immunospecifically bind to FGF-CX or any derivative, variant, mutant, or fragment of the FGF-CX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the FGF-CX polypeptide, polynucleotide and antibody are used in detection and treatment of [a broad range of] pathological states[, as well as to other uses].

Replace page 81 with substitute page 81 attached as Appendix C.

Appendix B: Version Marked to Show Changes Made in Claims

In the claims:

Cancel claims 3 and 6 without prejudice and without disclaimer of the subject matter.

Withdraw Claim 21 from further examination without prejudice and without disclaimer, as being directed to a non-elected invention.

Amend claims 1, 5, 14, 19-20, 28-29 as indicated below.

1. (Amended) An isolated FGF-CX nucleic acid molecule encoding [FGF-CX, said molecule comprising a nucleotide sequence encoding] a polypeptide [having] comprising a sequence [that is at least 85% identical to] of SEQ ID NO:2, or the complement of said nucleic acid molecule.

5. (Amended) The isolated nucleic acid molecule of claim 1, said molecule encoding [a polypeptide comprising] the amino acid sequence of SEQ ID NO:2, [or an] said amino acid sequence further comprising one or more conservative amino acid substitutions [in the amino acid sequence of SEQ ID NO:2], wherein said substitutions do not alter the functional ability of the FGF-CX protein.

14. (Twice Amended) A method of producing an isolated FGF-CX [polypeptide at least 80% identical to a] polypeptide of SEQ ID NO:2, said method comprising the step of culturing the host cell of claim 10 under conditions in which the nucleic acid molecule is expressed.

19. (Twice Amended) A pharmaceutical composition comprising [a therapeutically or prophylactically effective amount of] the nucleic acid of claim 1, and a pharmaceutically acceptable carrier.

20. (Amended) A kit comprising in one or more containers, [a therapeutically or prophylactically effective amount of the pharmaceutical] the composition of claim 19.

28. (Amended) An isolated nucleic acid molecule [encoding FGF-CX, said molecule] comprising a [nucleotide sequence selected from the group consisting of:

a) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO:1;

b) a fragment of a nucleic acid sequence sequence comprising a nucleic acid sequence of SEQ ID NO:1, wherein the fragment comprises at least 6 contiguous nucleotides of SEQ ID NO: 1;

c) a derivative of a nucleic acid comprising a nucleic acid of SEQ ID NO: 1;

d) an analog of a nucleic acid comprising a nucleic acid of SEQ ID NO: 1;

e) a homolog of a nucleic acid comprising a nucleic acid of SEQ ID NO: 1; or

f) a naturally occurring allelic variant of a nucleic acid comprising a] nucleic acid of SEQ ID NO: 1, wherein the nucleic acid hybridizes to a nucleic acid molecule of SEQ ID NO: 1 under stringent conditions.

29. (Amended) The nucleic acid of claim 28 [wherein the nucleic acid, or a fragment thereof,] encoding the polypeptide of SEQ ID NO: 2 [has] having an activity selected from the group consisting of:

a fibroblast growth factor-like activity;

a cell proliferative activity;

a glia activating activity; and

a neuroprotective-like activity.

Appendix C: Replacement page for Abstract

ABSTRACT

The present invention provides FGF-CX polypeptides and polynucleotides, and antibodies that immunospecifically bind to FGF-CX or any derivative, variant, mutant, or fragment of the FGF-CX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the FGF-CX polypeptide, polynucleotide and antibody are used in detection and treatment of pathological states.